

II. REMARKS

Formal Matters

Claims 1-21 are pending after entry of the amendments set forth herein.

Claims 1-20 were examined and were rejected.

Claims 5 and 12 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claims 5 and 12 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary location: paragraph 0047. Accordingly, no new matter is added by these amendments.

Claim 21 is added. Support for new claim 21 is found in the claims as originally filed, and throughout the specification, including the following exemplary location: paragraph 0047. Accordingly, no new matter is added by new claim 21.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Allowable subject matter

Applicants note with gratitude that claims 10 and 13-15 would be allowable if re-written in independent form, including all of the limitations of the base claim and any intervening claims.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-20 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

Requirement under 35 U.S.C. §112, second paragraph

All that is required under 35 U.S.C. §112, second paragraph, is that a claim set out the subject matter with a reasonable degree of clarity and particularity, such that the scope of the claim is clear to a person of ordinary skill in the relevant art.

Claim 1

The Office Action stated that it is unclear if the isolated apoE stable folding intermediate is natural or man made. Applicants respectfully traverse the rejection.

There is no requirement under 35 U.S.C. §112, second paragraph, that a claim specify whether an isolated compound is natural or man made. There is no need to specify whether the isolated apoE is natural or man made in order to apprise a person of ordinary skill in the art of the claim scope. As such, claim 1 is in compliance with the requirements of 35 U.S.C. §112, second paragraph, and need not be amended.

Claim 5

The Office Action stated that it is unclear whether a manual or automated technique is required for step (b).

There is no requirement under 35 U.S.C. §112, second paragraph, that a claim reciting a “determining” step specify whether the technique used is manual or automated. There is no need to specify whether the method used is manual or automated in order to apprise a person of ordinary skill in the art of the claim scope. As such, claim 5 is in compliance with the requirements of 35 U.S.C. §112, second paragraph, and need not be amended.

Claim 12

The Office Action stated that the metes and bounds intended for “in a solution” cannot be determined.

Claim 12 recites “contacting an apoE stable folding intermediate in a solution with a test agent.” Those of ordinary skill in the art would understand the meaning of “in a solution” in this context. As such, claim 12 is in compliance with the requirements of 35 U.S.C. §112, second paragraph, and need not be amended.

Conclusion as to the rejections under 35 U.S.C. §112, second paragraph

Applicants submit that the rejections under 35 U.S.C. §112, second paragraph, have been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C. §102(b)

Claims 1-4 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Morrow et al. ((September 26, 2000) *Biochem.* 39:11657-11666; “Morrow”).

The Office Action stated that Morrow discloses a composition comprising an isolated apoE folding intermediate. Applicants respectfully traverse the rejection.

Morrow does not disclose an isolated apoE stable folding intermediate. Morrow states that guanidine-HCl denaturation of apoE monitored by circular dichroism and fluorescence suggested the presence of a folding intermediate in apoE. Morrow, Abstract. However, a stable folding intermediate was not isolated.

In contrast, in the instant application, conditions were determined for generating compositions comprising an isolated apoE stable folding intermediate. For example, the instant specification indicates that an apoE stable folding intermediate is produced in significant amounts in conditions of about 2 M to about 7 M urea. Specification, paragraph 0049. The isolated apoE stable folding intermediate is isolated, e.g., at least about 60%, 70%, 80%, 85%, or more. pure. Specification, paragraph 0047.

Morrow does not disclose an isolated apoE stable folding intermediate. Accordingly, Morrow cannot anticipate any of claims 1-4.

Conclusion as to the rejection under 35 U.S.C. §102(b)

Applicants submit that the rejection of claims 1-4 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejections under 35 U.S.C. §103(a)

Claims 5-9, 11, 12, and 16-18 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Roses et al. (U.S. Patent No. 6,027,896; “Roses”) in combination with Morrow. Claims 16, 17, 19, and 20 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Poirier (U.S. Patent No. 6,022,683; “Poirier”) in combination with Morrow.

Requirements to establish a prima facie case of obviousness

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 21 USPQ2d 1941 (Fed. Cir. 1992). Second, there must be a reasonable expectation of success. *In re Merck & Co., Inc.*, 231 USPQ 375 (Fed. Cir. 1986). Finally, the prior art reference, or references when combined, must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA 1974). All three criteria must be met. If any one of these three criteria is not met, a *prima facie* case of obviousness has not been established.

Claims 5-9, 11, 12, and 16-18 over Roses in combination with Morrow

The Office Action stated that: 1) Roses discloses a method for determining the activity of apoE4; 2) Roses discloses diagnosing Alzheimer's Disease in a subject by detecting the presence of apoE4; 3) Roses does not disclose an apoE stable folding intermediate; 4) Morrow discloses an isolated apoE folding intermediate. The Office Action concluded that it would have been obvious to provide a method of treating apoE-related disorder as claimed because "Roses et al disclose the invention claimed except for addressing a nexus between an apoE folding intermediate and apoE4 that was provided by Morrow et al (Abstract Only)." Office Action, page 4. Applicants respectfully traverse the rejection.

The Office Action has not established a prima facie case of obviousness. There is no motivation to combine the reference teachings. There is no reasonable expectation of success in the cited references. The cited references do not teach or suggest all of the claim limitations.

1. There is no motivation to combine the references.

In making an obviousness rejection, the Office must articulate the basis on which it concludes that it would have been obvious to make the claimed invention. This requires that the Office explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious. The Office Action has not provided any such reasons.

There is no suggestion or motivation, either in the cited references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references. Roses relates to a method of diagnosing Alzheimer's Disease by detecting the presence of an apoE4 isoform,

or DNA encoding apoE4 in a subject. There is no mention in Roses of any apoE stable folding intermediate. There is no mention in Roses of use of an isolated apoE stable folding intermediate to identify agents that modulate its lipid binding activity or levels. Roses is concerned with detecting apoE4, not modifying its function or level.

Morrow does not provide any motivation to combine. Morrow does not disclose or suggest an isolated apoE stable folding intermediate. Morrow does not disclose conditions for generating an isolated apoE stable folding intermediate. Morrow discusses the p Morrow does not disclose or suggest any method of use of an isolated apoE stable folding intermediate to identify agents that modulate its lipid binding activity or levels.

2. There is no reasonable expectation of success.

There is no mention in Roses of any apoE stable folding intermediate. There is no mention in Roses of use of an isolated apoE stable folding intermediate to identify agents that modulate its lipid binding activity or levels. Thus, Roses cannot have provided a reasonable expectation of success in carrying out a subject method.

Morrow does not disclose conditions for generating an isolated apoE stable folding intermediate. Thus, Morrow cannot have provided a reasonable expectation of success in carrying out a subject method.

3. The cited references do not teach or suggest all of the claim limitations.

Roses neither discloses nor suggests a method of identifying an agent that reduces lipid binding activity of an apoE stable folding intermediate, or a method of identifying an agent that reduces the level of an apoE stable folding intermediate, the methods involving contacting an isolated apoE stable folding intermediate in a solution with a test agent. Roses neither discloses nor suggests a method of treating an apoE-related disorder comprising reducing the level and/or activity of an apoE stable folding intermediate.

Roses does not mention an isolated apoE stable folding intermediate, and how such might be used in identifying agents that affect its lipid binding activity or its level.

Morrow does not cure the deficiency of Roses. As discussed above, Morrow does not teach an isolated apoE stable folding intermediate. Morrow does not disclose or suggest conditions that would provide for a composition comprising an isolated apoE stable folding intermediate. Accordingly, Roses, alone or in combination with Morrow, does not teach or suggest all of the claim limitations.

In view of the discussion above, Roses, alone or in combination with Morrow, cannot render any of claims 5-9, 11, 12, and 16-18 obvious.

Claims 16, 17, 19, and 20 over Poirier in combination with Morrow

The Office Action stated that: 1) Poirier discloses treating an apoE-related disorder by administering a pharmaceutical; 2) Poirier does not disclose an apoE folding intermediate; and 3) Morrow discloses a nexus between an apoE folding intermediate and apoE isoforms. The Office Action concluded that it would have been obvious to provide a method of treating an apoE-related disorder as claimed because “Poirier discloses the invention claimed except for addressing a nexus between an apoE folding intermediate and apoE isoform that was provided by Marrow et al. (Abstract Only).” Office Action, page 6. Applicants respectfully traverse the rejection.

Neither Poirier nor Morrow provides any disclosure or suggestion whatsoever of a method of treating an apoE-related disorder by reducing the level and/or activity of an apoE folding intermediate. Poirier, alone or in combination with Morrow, cannot render any of instant claims 16, 17, 19, or 20 obvious.

Poirier makes no mention whatsoever of any apoE stable folding intermediate. Poirier neither discloses nor suggests a method of treating an apoE-related disorder, involving reducing the level and/or activity of an apoE stable folding intermediate.

Morrow does not cure the deficiency of Poirier. Morrow does not discuss reducing the level and/or activity of an apoE stable folding intermediate. Morrow does not provide any indication that reducing the level and/or activity of an apoE stable folding intermediate will treat an apoE-related disorder. Accordingly, Poirier, alone or in combination with Morrow, cannot render any of instant claims 16, 17, 19, or 20 obvious.

Conclusion as to the rejections under 35 U.S.C. §103(a)

Applicants submit that the rejections of the claims discussed above under 35 U.S.C. §103(a) have been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

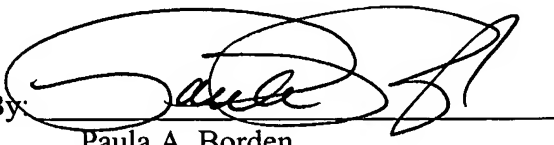
III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-282.

Respectfully submitted,
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Date: Apr. 17, 2006

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